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# Brain activity elicited by viewing pictures of the own virtually amputated body predicts xenomelia

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ABSTRACT

*Background:* Xenomelia is a rare condition characterized by the persistent desire for the amputation of physically healthy limbs. Prior studies highlighted the importance of superior and inferior parietal lobuli (SPL/IPL) and other sensorimotor regions as key brain structures associated with xenomelia. We expected activity differences in these areas in response to pictures showing the desired body state, i.e. that of an amputee in xenomelia.
*Methods:* Functional magnetic resonance images were acquired in 12 xenomelia individuals and 11 controls while they viewed pictures of their own real and virtually amputated body. Pictures were rated on several dimensions. Multivariate statistics using machine learning was performed on imaging data.
*Results:* Brain activity when viewing pictures of one's own virtually amputated body predicted group membership accurately with a balanced accuracy of 82.58% ($p = 0.002$), sensitivity of 83.33% ($p = 0.018$), specificity of 81.82% ($p = 0.015$) and an area under the ROC curve of 0.77. Among the highest predictive brain regions were bilateral SPL, IPL, and caudate nucleus, other limb representing areas, but also occipital regions. Pleasantness and attractiveness ratings were higher for amputated bodies in xenomelia.
*Conclusions:* Findings show that neuronal processing in response to pictures of one's own desired body state is different in xenomelia compared with controls and might represent a neuronal substrate of the xenomelia complaints that become behaviourally relevant, at least when rating the pleasantness and attractiveness of one's own body. Our findings converge with structural peculiarities reported in xenomelia and partially overlap in task and results with that of anorexia and transgender research.

## 1. Introduction

Xenomelia (McGeoch et al., 2011), also known as body integrity identity disorder (First, 2005; First and Fisher, 2012) or apotemnophilia (Brang et al., 2008), is an unusual and rare condition in which sufferers express the persistent desire for the amputation of limb(s) that are physically fully functioning. Xenomelia individuals typically report that their unwanted limb(s) do not belong to themselves and that they would feel better if the limb(s) were to be removed (Blanke et al., 2009). Psychiatric and neurocognitive assessments of xenomelia individuals reveal no known disease that could account for the amputation desire, and especially the absence of psychotic disorders has been repeatedly reported (Blom et al., 2012; Brugger and Lenggenhager, 2014; First, 2005; Hilti et al., 2013; van Dijk et al., 2013).

Since it has been proposed that xenomelia might be a neurological disorder (Brang et al., 2008; McGeoch et al., 2011), particularly a new right parietal lobe syndrome (McGeoch et al., 2011), there is growing evidence that both brain structure (Blom et al., 2016; Hänggi et al., 2016, 2017; Hilti et al., 2013) and brain function (Hänggi et al., 2017; McGeoch et al., 2011; van Dijk et al., 2013) differ between xenomelia individuals and controls as reviewed elsewhere (Brugger et al., 2016).

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There is evidence that social components might play a role in the condition as well (Brugger et al., 2013).

Structural and functional neuroimaging studies in xenomelia revealed that the right superior (SPL) and inferior parietal lobule (IPL) (Hänggi et al., 2017; Hilti et al., 2013; McGeoch et al., 2011; van Dijk et al., 2013), right anterior insula (Brang et al., 2008; Hilti et al., 2013), and right primary and secondary somatosensory cortex (SI and SII, respectively) (Hilti et al., 2013; van Dijk et al., 2013), particularly its left leg representation (Hänggi et al., 2017; Hilti et al., 2013) are altered in the condition compared with controls. The paracentral lobule, supplementary motor area, basal ganglia, thalamus, and the cerebellum (Blom et al., 2016; Hänggi et al., 2016, 2017) are additionally altered in xenomelia.

Taken together, there is strong evidence that many areas of the sensorimotor system and the insula are altered in xenomelia individuals as revealed by anomalies in cortical thickness and surface area derived from surface-based morphometry (Hilti et al., 2013). Differences in the magnetoencephalographic signal (McGeoch et al., 2011) and neuronal activity measured with functional magnetic resonance imaging (fMRI) (van Dijk et al., 2013) in response to tactile stimulation have been reported as well. Anomalies have also be found in structural and functional connectivity derived from diffusion tensor imaging-based fibre tractography and seed-to-seed-based correlation analyses of resting state fMRI data, respectively (Hänggi et al., 2017), and in thalamic, putaminal, and pallidal shape (Hänggi et al., 2016).

Intriguingly, all these brain regions are associated with the construction and the maintenance of a coherent body image (Berlucchi and Aglioti, 2010; Gerardin et al., 2003; Giummarra et al., 2008; Moseley et al., 2012; Tsakiris et al., 2007; Wolbers et al., 2003). Investigations of healthy human subjects provide strong evidence that both SPL and IPL mediate body ownership (Kammers et al., 2009) and are key for the integrative mental imagery of the configurations of limbs (Wolbers et al., 2003). In particular the right-hemispheric SPL was involved in monitoring illusory limb displacements, independent of the limb's laterality (Naito et al., 2005). In addition, primary and secondary somatosensory hand representations are crucial in mediating the illusion of a rubber hand, where the visual observation of a rubber hand being touched simultaneously with the experience of touch to one's own hand evokes the sensation of an incorporation of the rubber hand (Tsakiris et al., 2007) and leads to a diminished animation of the real hand (Moseley et al., 2008). With respect to the homeostatic state of the body and interoceptive awareness, the insula predominately in the right hemisphere is key for establishing and maintaining the sense of body ownership (Craig, 2009, 2011; Critchley et al., 2004; Karnath and Baier, 2010; Moseley et al., 2012).

Here, we investigated the neuronal response to different types of body-related pictures showing either one's own desired body state or one's own undesired body state. Similar paradigms as the one used here have already been applied to anorexia nervosa patients and transgender individuals (Feusner et al., 2016; Fladung et al., 2010). For that purpose, to our knowledge for the first time, individual stimuli comprising photos of one's own body (and a control body as well) in different positions were constructed and edited according to the individual amputation desire of the xenomelia subjects. We compared 12 xenomelia individuals with 11 male controls with respect to whole-brain functional activity when viewing these body-related pictures. Activity was measured with fMRI in response to six different categories of body-related pictures: the real own body/a control body, the own body virtually amputated/a control body virtually amputated, and the own body virtually amputated with prosthesis/control body virtually amputated with prosthesis. Subsequently to the fMRI session, these pictures were also rated with respect to pleasantness, intensity, attractiveness and sexual arousal.

We hypothesized that viewing the desired state of one's own body, i.e. that of an amputee in xenomelia and that of a non-amputated body in controls, evokes differential brain activity compared with brain activity when viewing one's own undesired body state, i.e. a non-amputated body in xenomelia and an amputated body in controls. Differential brain activity is expected to be present mainly in brain regions associated with the construction and maintenance of a coherent body image such as the parietal cortices (SPL and IPL), but also in brain regions housing limb representations such as the primary and secondary somatosensory cortex, basal ganglia, thalamus, premotor cortex, supplementary motor area as well as the insular cortex that is key for the homeostatic state of the body and interoceptive awareness. It has already been shown that all these brain regions are structurally and/or functionally conspicuous in xenomelia subjects as reviewed elsewhere (Brugger et al., 2016).

In addition to the brain regions associated with body representations, we also expected differential brain activity in limbic regions associated with emotional processing due to the fact that viewing the desired or undesired body state also elicits differential affective states. With respect to the direction of effects and based on the small corpus of the functional neuroimaging literature in this condition, we expected increased as well as reduced activity in xenomelia compared with healthy male controls (Hänggi et al., 2017; McGeoch et al., 2011; van Dijk et al., 2013).

## 2. Subjects, materials and methods

### 2.1. Subjects

Thirteen male individuals with xenomelia were recruited via Internet. One subject quit the fMRI session and withdrew from the study and was therefore excluded. The mean age of the remaining 12 individuals was 46.5 years (standard deviation (SD) = 11.6 years, range 32–68 years) and eight of them achieved a university degree. Nine individuals whished an amputation of the left leg (at the height of the thigh), one of the right leg, and the remaining two of both legs. Seven individuals were heterosexuals and five homosexuals. For nine of the 12 individuals, the desire for limb amputation also has a sexually arousing component.

Additionally, twelve healthy male controls were recruited. One control subject produced strong motion-related artefacts during fMRI and was therefore excluded. Mean age of the remaining 11 controls was 41.9 years (SD = 11.0 years, range 29–65 years) and eight of them achieved a university degree.

Inclusion criterion for xenomelia was the persistent desire for an amputation of one or both legs that has lasted since childhood (Brugger et al., 2016; First and Fisher, 2012). Exclusion criteria were MRI incompatibility or any psychiatric or neurological disorder other than xenomelia. All participants provided written informed consent. The study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics review board.

### 2.2. Psychiatric and psychometric assessments

The Brief Symptom Inventory (BSI) (Franke, 2000), which is a short form of the Symptom-Checklist-90-Revised (SCL-90-R) (Franke, 2002) was applied. It assesses the psychological strain with respect to different symptoms and consists of 53 items. Nine scales measure somatization, compulsivity, uncertainty in social contacts, depression, anxiety, aggression and hostility, phobic fear, paranoid thinking, and psychoticism. The three main global indices are the Global Severity Index (GSI), Positive Symptom Distress Index (PSDI) and Positive Symptom Total (PST). For analysis, the raw values of each BSI scale were added and then transformed into T-values and percent ranks. Values between 40 and 60 are not conspicuous. Test duration is about 7–10 min. The BSI and the SCL-90-R were applied only to the individuals with xenomelia. Control subjects were assessed for psychiatric or neurological disorders by the psychologists/medical doctor in our team in the early recruitment phase. We enrolled a short clinical anamnesis that revealed no